Case Report Rapport de cas

Emphysematous pyelitis and cystitis associated with vesicoureteral reflux in a diabetic dog

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Abstract — A 12-year-old female dog with a 3-month history of poor response to diabetes treatment had an acute worsening of symptoms, including weakness and blindness. The dog had elevated blood glucose, alkaline phosphatase and urea concentration, hyposthenuria, glycosuria, hematuria, and pyuria. *Escherichia coli* was isolated from the urine. Radiographs and ultrasound examination showed that the dog had unilateral emphysematous pyelitis and concurrent cystitis associated with vesicoureteral reflux.

Résumé — Pyélite emphysémateuse et cystite associées au reflux vésico-urétéral chez une chienne diabétique. Une chienne âgée de 12 ans avec une anamnèse de 3 mois de mauvaise réponse au traitement du diabète a présenté un aggravement aigu des symptômes, y compris de la faiblesse et de la cécité. La chienne avait une glycémie élevée, ainsi que des concentrations sériques élevées de la phosphatase alcaline et d'urée, de l'hyposthénurie, de la glycosurie, de l'hématurie et de la pyurie. *Escherichia coli* a été isolé de l'urine. Des radiographies et des échographies ont montré que la chienne était atteinte de pyélite emphysémateuse unilatérale et de cystite concomitante associées au reflux vésico-urétéral.

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Case description

We evaluated a 7 kg, 12-year-old, spayed female mixed-breed dog that had a 1-week history of general weakness, lethargy, and sudden onset of blindness. The patient had a 3-month history of uncontrolled diabetes mellitus with persistent polyuria, polydipsia, and weight loss. Previous abdominal ultrasonographic examination, performed 3 mo earlier, revealed no abnormalities of the urinary tract and the urine culture was negative. Upon initial physical examination, the dog was cachectic (body condition score: 2/9), moderately dehydrated, and had depressed mentation. Rectal temperature, arterial pulse rate, and quality and rate of respiration were all within normal ranges. Cataracts were present in both eyes. Hematologic evaluation showed anemia with 4.97×10^{12} red blood cells (RBCs)/L [reference range (RR): 5.50×10^{12} to 8.00×10^{12} RBCs/L] and a hematocrit of 32% (RR: 37% to 54%). Biochemical tests included serum glucose of 29.1 mmol/L (RR: 4.4 to 6.1 mmol/L), serum blood urea of 15.4 mmol/L (RR: 5.4 to 12.5 mmol/L), and alkaline phosphatase activity of 343 U/L (RR: 10 to 150 U/L). Analysis of urine collected by cystocentesis (performed under ultrasound guidance after the diagnostic imaging procedures) revealed a urine specific gravity of 1.020, glycosuria (4+), hematuria (2+) and pyuria, and the presence of hyaline casts and numerous bacteria. Venous blood gas analysis parameters were within normal ranges. A urine sample was submitted for culture and sensitivity testing.

Diagnostic imaging included radiographic and ultrasonographic examination of the abdomen. Evidence of intraluminal gas accumulation within the urinary bladder was detected on plain radiographs (Figures 1A, B). However, there was no radiolucent circumference zone in the bladder, indicative of intramural gas. Mild loss of serosal detail was noted, compatible with the presence of a small amount of abdominal effusion or with lack of fat in an emaciated patient. Lumbar spondylosis was detected as an incidental finding at L1–L2 and L2–L3.

Abdominal ultrasound examination showed a hyperechoic interface in the non-dependent portion of the bladder with multiple reverberation artifacts, consistent with a large amount of gaseous intraluminal content (Figure 2A). A small amount of intramural gas was seen as a hyperechoic interface with multiple reverberation artifacts in the cranio-ventral bladder wall (Figure 2B). By scanning the patient in both standing and recumbent positions, the gas was confirmed to be intramural, as a hyperechoic line was present in the ventral bladder wall. Hyperechoic foci were present in the bladder lumen, moving to the dependent part of the bladder wall, likely representing cellular debris. A dilation of the left renal pelvis of 2.5 mm and multiple hyperechoic foci with ring-down artifacts in the collecting system, compatible with gas bubbles, were detected (Figure 3A). The left renal cortex was slightly hyperechoic

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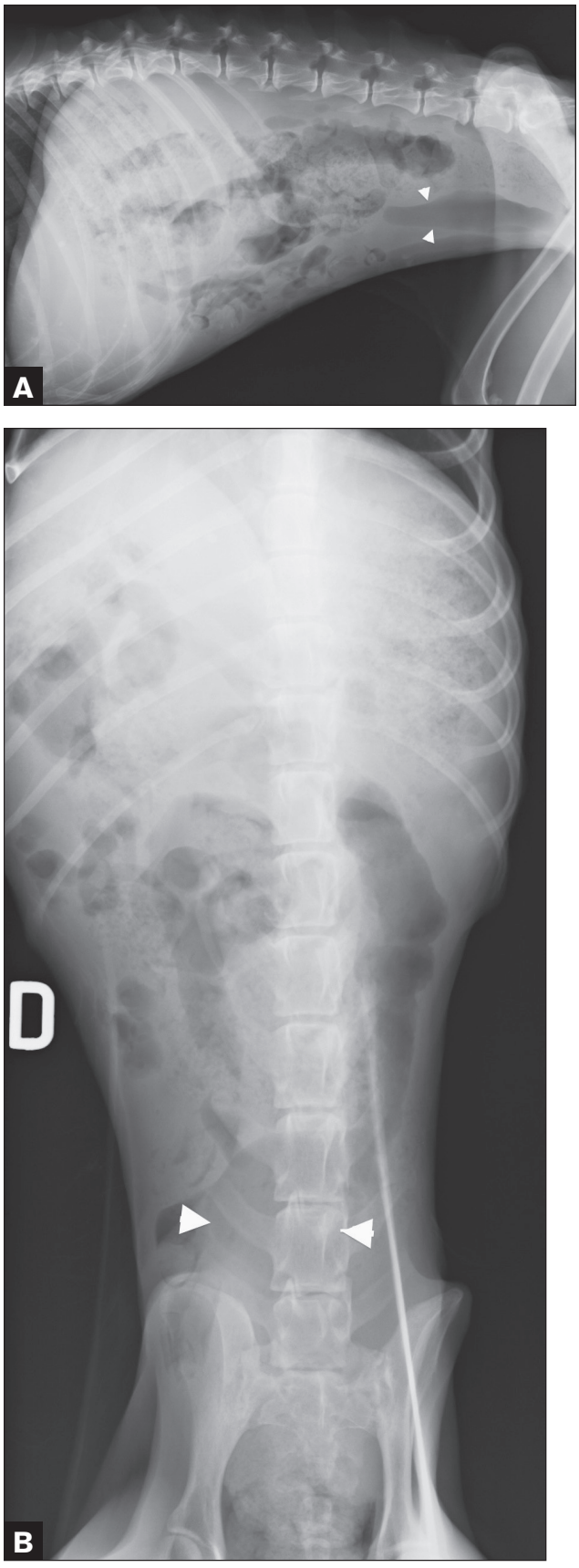

Figure 1. Lateral (A) and ventrodorsal (B) radiographic views of the abdomen of the patient. Gas within the bladder lumen was easily detected (arrowheads), but no signs of gas were seen in the bladder wall, kidneys, or retroperitoneal space.

compared to the spleen, but no gas was visible in the renal parenchyma. A clear demarcation between the left renal cortex and medulla was maintained. The left ureter was diffusely dilated, with a maximum diameter of 4.4 mm. Hyperechoic foci were seen within the ureteral lumen, associated with multiple ring-down artifacts, moving towards the renal pelvis, consistent with vesicoureteral reflux (Figure 3B). The right renal pelvis was dilated 2.2 mm. The right renal cortex was mildly hyperechoic with normal corticomedullary demarcation. Neither right ureteral dilation nor signs of intraluminal gas was seen. The liver was mildly hyperechoic with coarse parenchymal echotexture. A small amount of abdominal anechoic effusion was present. The remainder of the ultrasound examination was unremarkable.

Based on blood tests, urinalysis, and image abnormalities, a tentative diagnosis of emphysematous cystitis and concurrent unilateral emphysematous pyelitis, associated with vesicoureteral reflux was made.

The dog was hospitalized and received intravenous fluid therapy with 0.9% sodium chloride solution supplemented with potassium (40 mEq/L) to correct dehydration. Pending results of urine culture and sensitivity testing, antibiotic therapy with enrofloxacin (Baytril; Bayer Animal Healthcare, Garbagnate Milanese, Milano, Italy), 5 mg/kg body weight (BW), SC, q24h, was initiated. A low dose of regular insulin was administered by constant rate infusion (0.05 to 0.1 U/kg BW per hour) and treatment was adjusted based on serial measurements of serum electrolytes, glucose concentration, and blood gas analysis.

Although *Escherichia coli* cultured from the urine was susceptible to enrofloxacin, the patient's clinical condition worsened. The dog died 2 d after hospitalization. The owners declined necropsy.

Discussion

Emphysematous urinary tract infections are rare in humans and animals (1,2). In humans, in the absence of iatrogenic manipulation and fistulous connection with a hollow viscus, the spontaneous appearance of gas within the urinary tract may be caused by gas-forming infections of the genitourinary tract (3). Humans with diabetes mellitus, neurogenic bladder, urinary tract obstruction, vesicoureteral reflux, and recurrent urinary tract infections are at increased risk for emphysematous urinary tract infections (4). Moreover, middle-aged, diabetic women are at a significantly higher risk for disease (5).

In dogs, emphysematous urinary tract infections have been reported mainly in diabetic patients (6,7). However, a few cases of emphysematous cystitis have been described in non-glycosuric dogs due to chronic urinary tract infections, bladder trigone diverticulum, and long-term administration of steroids (8–11). No gender predisposition has been reported in dogs or cats (1).

Emphysematous pyelitis and emphysematous pyelonephritis are thoroughly described in humans but rarely reported in small animals (1). In the veterinary literature, there are only 3 case reports of concurrent emphysematous cystitis and bilateral emphysematous pyelonephritis and 2 of these occurred in diabetic patients (a cat and a dog) (1,7). To our knowledge, this is the first reported case of emphysematous pyelitis and cystitis associated with vesicoureteral reflux in a dog.

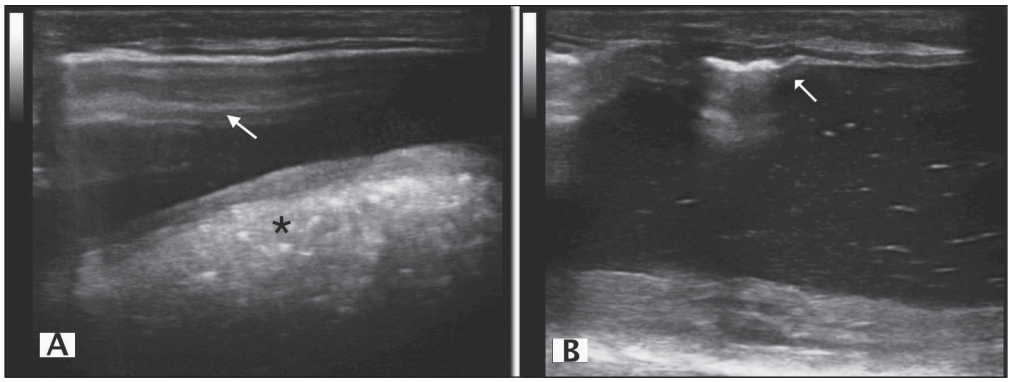

Figure 2. Sagittal ultrasonographic image of the bladder of the dog in dorsal recumbency (A) and in standing position (B). A – A hyperechoic interface with reverberation artifacts, consistent with a large amount of gas in the non-dependent part of the lumen (arrow). The descending colon is seen in the far field (asterisk). B – A hyperechoic stripe is visible in the cranio-ventral aspect of the bladder wall, with multiple reverberation artifacts, compatible with intramural gas (arrow). Echogenic material is present in the urinary bladder consistent with either cellular or proteinaceous debris.

In humans, emphysematous pyelonephritis is a severe gas-forming infection of the renal parenchyma or perirenal tissues and has a high mortality rate. High tissue glucose levels, impaired tissue perfusion, and a defective immune response all seem to be involved in the pathogenesis of this condition (12). Diabetics account for up to 90% of all cases and 100% of the cases of bilateral emphysematous pyelonephritis (13). Emphysematous pyelitis is defined as isolated gas production inside the excretory system secondary to acute bacterial renal infection (14) and is usually associated with a low mortality rate in humans. Emphysematous pyelitis is rarely reported, and is infrequently associated with emphysematous cystitis (2,14–16). Emphysematous pyelitis is more common in women (3:1) with a mean age of 51.

The pathogenesis of emphysematous urinary tract infections is not well understood, but it has been suggested that high tissue glucose levels in an immunocompromised host, such as a diabetic patient, can lead to infection with glucose-fermenting bacteria or yeast (17). Fermentation of substrates such as glucose and albumin within the urinary tract results in the formation of H_2 and CO_2 gas within the urinary tract and within the luminal mucosa (1,5,7).

Common bacterial causes of emphysematous infections in humans include *E. coli, Klebsiella pneumoniae,* and *Aerobacter* spp. (18). *Escherichia coli* is also commonly isolated in dogs and cats; other bacteria that are implicated are *Klebsiella* spp., *Proteus* spp., *Clostridium* spp., and *Aerobacter aerogenes* (1,8,19). The release of bacterial endotoxins may contribute to the inflammatory process, inducing paralysis of the urinary tract and urinary stasis (5). In this case report, left ureteral stasis may have caused urine reflux into the renal pelvis leading to emphysematous infection of the collecting system.

Diagnosis of emphysematous urinary tract infections is based on detection of gas in the renal excretory system by radiography, ultrasonography, and/or computed tomography (CT) in humans and animals (1–3,7,15). In the 3 reports of emphysematous pyelonephritis in veterinary patients, gas was readily identified within the entire urinary tract on radiographs (1,7). In our case, although a gas-filled urinary bladder was seen on survey abdominal radiographs, no sign of gas in the upper urinary tract was detected on films. It is likely that the small amount of gas related to unilateral emphysematous pyelitis rather than to bilateral emphysematous pyelonephritis, such as those previously reported, is difficult to identify on radiographs (1). The sensitivity of radiography reported in the human literature is low (33%) because of difficulty in differentiating renal gas from air in overlying loops of bowel (3,14,20). Moreover, radiography may not provide adequate morphologic information on the kidneys when the patient is emaciated, as was the case of the dog in our report, and has little value in the diagnosis of pyelonephritis and other disorders of the renal pelvis and ureter except for the identification of mineralized nephroliths (21). Ultrasound, however, can be useful for the detection of early cases of emphysematous infections in which there is only a small amount of radiographically inconspicuous gas (8).

In human medicine, a plain abdominal film called "KUB" (kidney, ureter, bladder) is recommended as a minimum radiographic screening tool to identify emphysematous urinary tract infections (22). However, for patients with severe urinary tract infections, particularly in diabetics, a rapid bedside ultrasound is strongly recommended for identifying stones and obstruction, as well as gas within the renal pelvis and calyces (3). Ultrasound findings of emphysematous pyelitis in humans include multiple bright echogenicities associated with posterior acoustic dirty shadowing within the renal sinus and anterior wall of the collecting system ("curtain like echoes") (3,14). The dirty shadow artifact is characterized by a chaotic display of continuous echoes extending throughout the visible field, with straight margins filling the entire field of view (23). The anatomic difference in the kidney collecting system of dogs (monopyramidal) and humans (multypyramidal) could have a role in the genesis of the different types of artifacts (24,25). The general impression is that gas in the upper urinary tract of small animals appears as discrete foci of echogenicity, producing periodic distal horizontal parallel lines (reverberations/ring down artifacts), rather than a chaotic appearance of echoes. Hyperechoic foci with reverberation

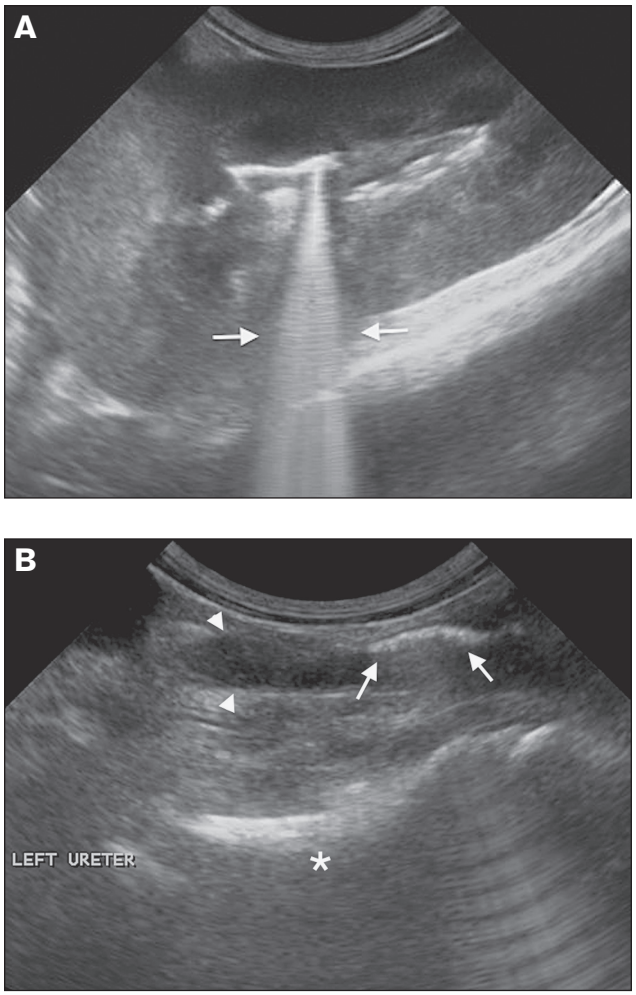

Figure 3. Sagittal ultrasonographic images of the left kidney (A) and the left ureter (B) of the dog. A – Reverberation artifacts within the pelvis (arrows). B – Left ureter appears dilated (arrowheads) and contains bright echoes in the non-dependent part of the lumen (arrows) indicating the presence of gas. The hyperechoic linear structure located deep and parallel to the ureter represents a lumbar vertebral body (asterisk).

artifacts in the renal cortex and collecting system of each kidney were described in a dog with emphysematous pyelonephritis (1).

In our case, hyperechoic foci associated with ring-down artifacts, moving through the dilated renal pelvis and ureter, were highly suggestive of the presence of gas. The presence of reverberations/ring-down artifacts, in the absence of distal dirty shadowing, may raise the suspicion of a minor amount of gas at the level of the renal pelvis in these veterinary patients. Reverberation and dirty shadowing are both ultrasound artifacts associated with the presence of gas. The presence of one or another depends on gas volume, gas location, and bubble structure (23). A small bubble cluster gives rise to a tapered distal artifact with periodic echogenicity (reverberations); a multiple layer of superimposed larger bubbles produces a bright field of echoes tails with different periods of occurrence and strength, forming the dirty shadowing artifact (23). These artifacts can be differentiated from the more distinct echo-free clean acoustic shadowing that occurs distal to renal calculi (14).

The most specific method for the diagnosis and monitoring of gas-containing infections of the urinary system in humans is CT (1,18). Computed tomography helps to exclude complicated forms of emphysematous pyelitis, such as the presence of renal or perirenal fluid collections, abscesses, or emphysematous pyelonephritis. Moreover, CT can rule out other causes of urinary gas such as vesicocolic fistula (26). Computed tomography can distinguish between the presence of gas bubbles within the pelvicalyceal system, the renal parenchyma, and/or the perinephric space (14,27).

In humans, emphysematous pyelonephritis and emphysematous pyelitis are distinct entities whose management and prognosis are different (2,27). Emphysematous pyelonephritis is treated aggressively with percutaneous drainage and antibiotics and, if necessary with nephrectomy. In the case of emphysematous pyelitis, if gas is localized in the collecting system and no obstruction is present, antibiotic therapy alone is usually sufficient (14,27).

The clinical and prognostic implications of emphysematous pyelitis and emphysematous pyelonephritis in dogs and cats are uncertain. Emphysematous cystitis, however, is considered a transient condition with a good prognosis provided that appropriate antibiotic therapy is given (8). Although the prognosis for human and veterinary patients with emphysematous cystitis is generally favorable, in human medicine, the standard is to consider this condition as a potentially fatal necrotizing infection that can rapidly ascend to the renal parenchyma if the diagnosis is delayed or if treatment is inadequate (5). Some authors even suggest a CT scan for human patients in whom gas accumulation within the urinary bladder lumen is revealed by plain radiography, as complicated conditions such as emphysematous pyelonephritis may need surgical intervention despite medical treatment (28).

It is also likely in veterinary medicine that early recognition of the disease is warranted in order to prevent progression of the infection to emphysematous pyelonephritis and urosepsis. The dog in this report showed gas in the bladder, left ureter, and corresponding renal pelvis, but not in the renal parenchyma or the perinephric space. These findings are consistent with emphysematous pyelitis. However, abdominal CT could not be performed and renal involvement of the infection was a possible sequela. Emphysematous pyelitis, along with uncontrolled diabetes mellitus, rapidly evolved into the death of the patient, despite antibiotic therapy. Although the use of CT for the diagnosis of emphysematous pyelitis or emphysematous pyelonephritis has not been reported in the veterinary literature, a CT scan of the abdomen could be useful to reveal the presence of gas bubbles in the renal parenchyma and in the upper urinary tract in dogs as in humans, but the risks associated with general anesthesia or sedation in debilitated canine patients should be carefully evaluated.

The rarity of emphysematous pyelitis in dogs, the association with emphysematous cystitis, and the presence of vesicoureteral reflux, are 3 significant characteristics described herein. A retrograde migration of microorganisms from the bladder to the kidney through a vesicoureteral reflux identified on ultrasound was the most likely underlying mechanism of emphysematous

upper urinary tract infection in this case. Conversely, in one of the other cases of emphysematous pyelonephritis in a dog with diabetes mellitus and associated hyperadrenocorticism, the emphysematous ureter and kidney changes were likely due to local fermentation rather than to gas accumulation in the urinary bladder and subsequent reflux (7).

Gas in the bladder lumen may be iatrogenically introduced, secondary to a fistulous connection with the intestine or genital tract or secondary to gas-producing bacteria (3). In this case the dog did not undergo bladder catheterization or vaginourethrography and cystocentesis was performed under ultrasound guidance at the end of the ultrasonographic examination. Moreover, the gas in the bladder was not limited to the lumen, as a small amount of it was seen in an intramural location. Although urethrorectal fistula could not have been excluded, it was considered unlikely. Fistulas are rare in dogs and cats, usually congenital, and associated with recurrent urinary tract infections (29). Finally, none of the dogs with urethrorectal fistula had signs of gas in the urinary bladder (29,30).

In conclusion, this is the first case of concurrent unilateral emphysematous pyelitis and emphysematous cystitis associated with vesicoureteral reflux in a diabetic dog reported in the veterinary literature. As diagnosis of upper urinary tract infection may be underestimated if only radiographs are carried out, ultrasonography should also be used in cases of suspected complicated urinary tract infections. If an emphysematous cystitis is detected on radiographs, an ultrasound scan of the upper urinary tract should be considered to detect emphysematous complications of kidneys and/or ureters. Guarded prognosis associated with emphysematous upper urinary tract infections in small animals warrants the consideration of more aggressive treatment options. However, further studies are necessary to define the real incidence of these conditions, their clinical implications and the correct management strategies in small animals. CVJ

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